The Histological Changes Induced by Indian Ginseng in Kidneys, Livers and Brains of Rats

Original Article

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ABSTRACT

Introduction: Herbal preparations are not adequately regulated. They are not subjected to the same production testing as chemical pharmaceuticals, and there are no standards like those found in medical drugs. As a result, utilizing them without constraints or circumstances may result in undesirable or harmful effects on multiple organs.

Aim of the Work: This study was carried out to look into some of the negative consequences of utilizing Ashwagandha (Indian ginseng) and its potential effects on the liver, kidneys, and brain.

Materials and Methods: 16 adult rats were randomly divided into two groups of eight each: the control group, which received distilled water daily with an injection volume of 1.0 ml/kg orally for 30 days, and the Indian ginseng-treated group, which received Indian ginseng root extract. Orally every day for 30 days at a dose of (200 mg/kg) diluted in (1.0 cc of distilled water). After the treatment time, the animals were sedated, and their liver, kidney, and brain organs were removed to study the histological alterations in those tissues.

Results: The treated group's liver sections revealed diffuse vacuolar degeneration of hepatocytes, inflammatory cell infiltration in the portal area, central vein congestion and hemosiderin staining, and congestion and dilatation of the central vein and portal vein with sinusoidal dilatation. While kidney slices from the same cohort revealed glomerular shrinkage, Bowman's space dilatation, localized inflammatory cell infiltration, and vascular congestion. Finally, portions of the treated group's brains revealed vacuolization edema and perivascular edema around neurons and glial cells.

Conclusion: We concluded that ashwagandha (ginseng) has a negative effect on various organs in rats at the concentration level utilized in the study.

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Key Words: Brains, indian ginseng, kidneys, rats livers.

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INTRODUCTION

Indian ginseng is a natural medication made from root extracts of Withania somnifera, a short-growing shrub native to India and Southeast Asia[1,2]. It is also a well-known and ancient herb in the East, where it was utilized as a tonic and cure for a variety of ailments due to its depressive and antioxidant characteristics[3]. It is also known as "Ashwagandha" and has been utilized as an Ayurvedic medication for decades, as well as a popular herbal treatment in Western countries[4]. According to certain studies, Indian ginseng contains anti-stress, neuroprotective, anti-tumor, anti-arthritic, anti-inflammatory, and analgesic properties[5,6].

Although the herb includes a variety of bioactive substances such as glycosides, flavonoids, steroids, alkaloids, and steroidal lactones, the molecules withanolides are responsible for the majority of the plant's effects[7,8]. However, very few studies have found that using ginseng may pose certain health hazards, necessitating additional research and analysis to prove these assumptions. According to an analysis of the negative effects of Indian ginseng reported in some research, a high concentration of Indian ginseng extract (Ashwagandha) still has limitations on the use of this type of plant, particularly allergies from the nightshade family[9]. According to one study, administering Ashwagandha extracts in low quantities to animals for an extended period of time produced no negative effects leading to withdrawal symptoms[10]. This study was meant to demonstrate the presence of adverse effects of Indian ginseng on specific organs in rats at the specified concentrations.

MATERIALS AND METHODS

The animals

The study used sixteen male Wester albino rats who were 8-10 weeks old and weighed 200-250 grams on average. The rats were confiscated from the Animal House Veterinary College at Mosul University in Iraq. All rats were housed at room temperature (22 2°C) with a 12-hour light-dark cycle and free access to water and food[11].

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Ethical approval

All procedures were carried out in accordance with the rules established by the Research Ethics Committee of the College of Dentistry at the University of Mosul in Iraq, using the code (UOM.Dent. 23/4).

Materials

The powdered Indian ginseng extract utilized in this investigation was sourced from the Turkish business "Naturalaya Kimya." For 30 days, Rat was administered an Indian ginseng solution orally on a daily basis[12].

Experimental design

Sixteen animals were divided into two groups at random: Group A (control), (n = 8): From the first day of the study, rats received daily distilled water with an injection volume (1.0 ml/kg) orally for 30 days using a gavage needle. Experiment until the end of the day (Figure A). Treatment with Indian ginseng (Group B), (n = 8): Rats were given Indian ginseng root extract daily and orally for thirty days using a gavage needle (200 mg/kg diluted in 1.0 ml of distilled water). From the first to the last day of the trial[13] (Figure B).

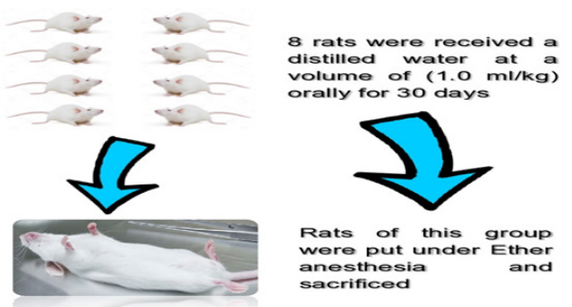

Fig. A: Illustrations for material and method

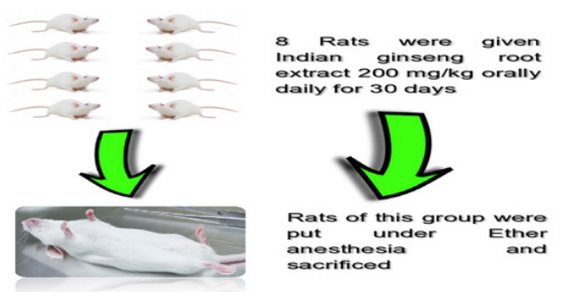

Fig. B: Illustrations for material and method

Sample collection

Each group of animals was anesthetized with "ether anesthesia" and then animal sacrifice at the end of the experiment, 2 hours after the last dose[13]. For the final histological analysis, liver, kidney, and brain parts were removed from deceased rats and put in 10% buffered formalin[14].

Tissue processing

Ethanol was used to dehydrate kidney, liver, and brain tissues for 1 hour at increasing concentrations (70%, 80%, 90%, and 100%). Following dehydration, tissue slides were removed using two different xylene changes (1 hour each). The tissue fragments were then immersed in three changes of melted paraffin wax at 60°C for one hour[14]. Following that, the slides were placed within paraffin blocks, and 5-m-thick sections were obtained from each tissue block using a Reichert Rotatory Microtome. The sections were then mounted on glass slides and deparaffinized in two xylene changes for 5 minutes each, followed by Set descending ethanol grades (absolute, 90%, 80%, 70%) for 2 minutes at each grade. Finally, hematoxylin and eosin-stained tissue sections were examined using a light microscope (B-15 OPTICA)[15].

RESULTS

Liver tissue

The histological features of liver sections in the control group (Group A) were normal with light microscopic inspection, indicating normal histological structure of the liver as central vein, portal area, sinusoids and hepatocytes (Figures 1 A,B).

Sections of liver from the Indian ginseng-treated group (group B) (Figures 1 C,D) revealed extensive vacuolar degeneration of hepatocytes, inflammatory cell infiltration in the portal area, central vein congestion, and hemosiderin staining. In addition to coagulative necrosis of hepatocytes, infiltration of polymorphonuclear inflammatory cells and mononuclear cells in the portal area, and eosinophilic cytoplasmic deposition of hepatocytes, these sections showed congestion and expansion of the central vein, portal vein and sinusoidal. There is also congestion of the portal vein (Figures 2 A,B,C).

Kidney tissue

In the control group (Group A), the histological structure of kidney sections was obviously typical, with normal glomeruli, distal renal tubules, and proximal renal tubules (Figures 3 A,B).

Kidney sections from the Indian ginseng-treated group (group B) revealed glomerular atrophy, Bowman's space dilatation, localized inflammatory cell infiltrate, vascular congestion, and coagulative necrosis of the renal tubule epithelial cells (Figures 3 C,D).

Brain tissue

With light microscopic examination, the histological sections of the brain sections of the control group (Group A) were clearly normal, as we could see the normal structure of the brain tissue represented by normal neurons, glial cells, and blood vessels (Figures 4 A,B). Brain slices from the Indian ginseng-treated group (Group B) revealed discharge edema around neurons and glial cells, as well as perivascular edema (Figure 4 C,D).

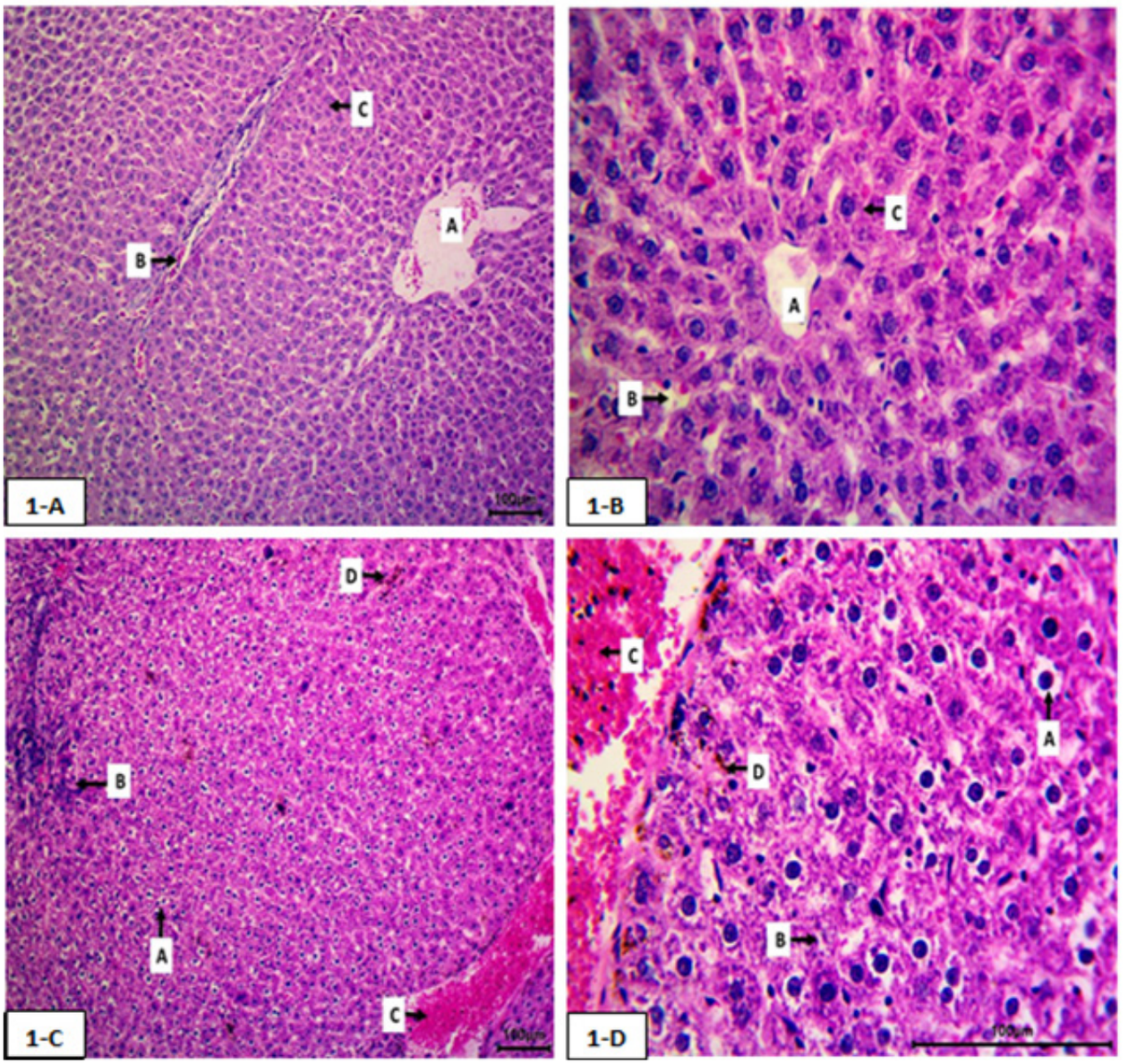

Fig. 1: photomicrograph of rats' liver tissues (1-A&B): control group showing normal architecture representing by central vein (A), portal area (B) (in 1-A), sinusoids (B) (in 1-B) and hepatocytes (C). (1-C&D): Indian Ginseng treated group showing diffuse vacuolar degeneration of hepatocytes (A), inflammatory cells infiltrations in portal area (B), congestion of central vein (C) and hemosiderin pigmentation (D). H&E stain (A&C:100X, B&D: 400X).

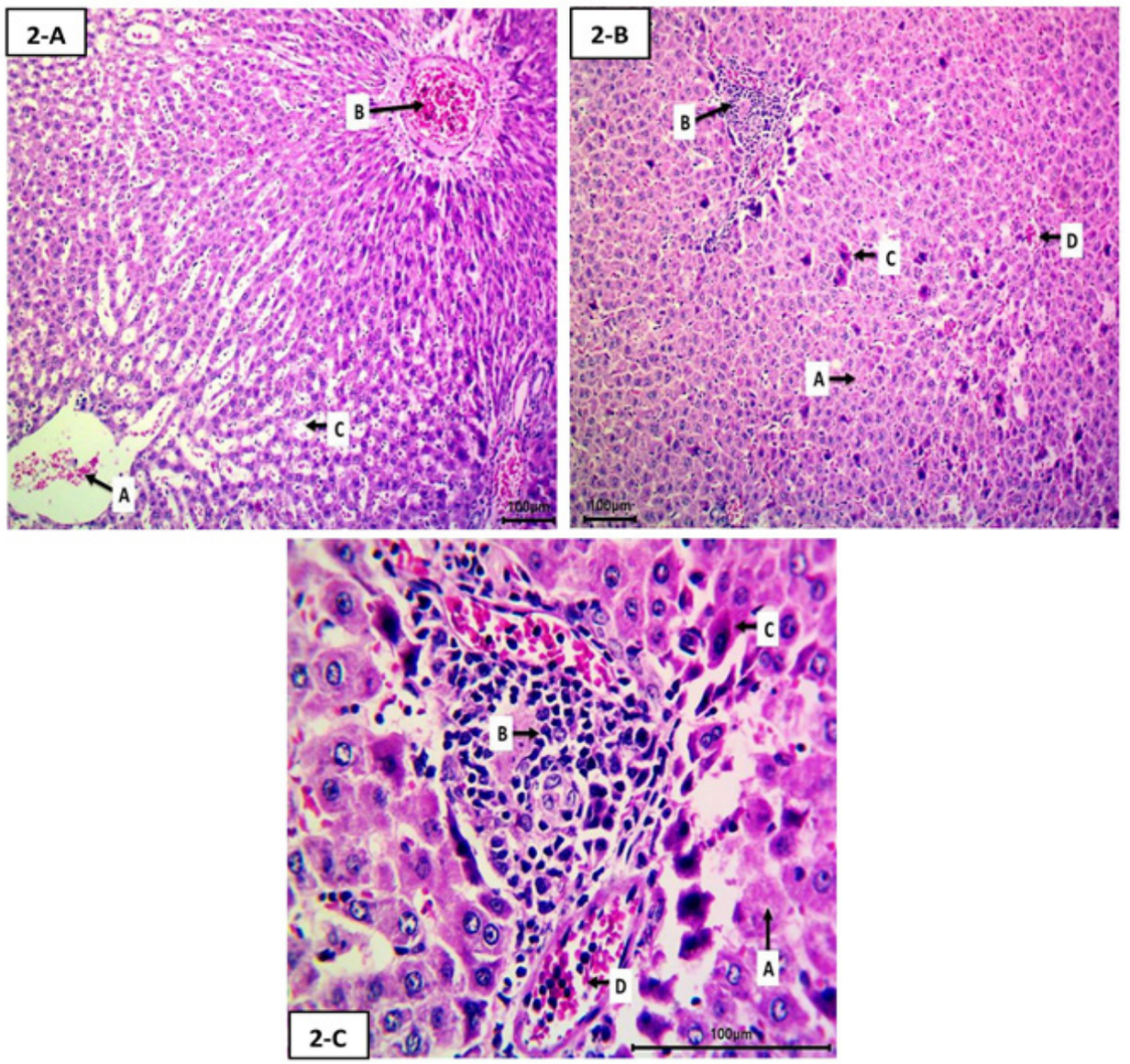

Fig. 2: photomicrograph of rats' liver tissues (2-A): Indian Ginseng treated group showing congestion and expansion of the central vein (A), portal vein (B), and expansion of sinusoids (C). (2-B): Indian Ginseng treated group showing mild coagulative necrosis of hepatocytes (A) focal inflammatory cells infiltrations in portal area (B), eosinophilic cytoplasmic deposition of hepatocytes (C) and congestion and expansion of sinusoids (D). (2-C): Indian Ginseng treated group showing coagulative necrosis of hepatocytes (A) focal polymorph and mononuclear inflammatory cells infiltrations in portal area (B), eosinophilic cytoplasmic deposition of hepatocytes (C) and congestion of portal vein (D). H&E stain, (A&B:100X, C: 400X).

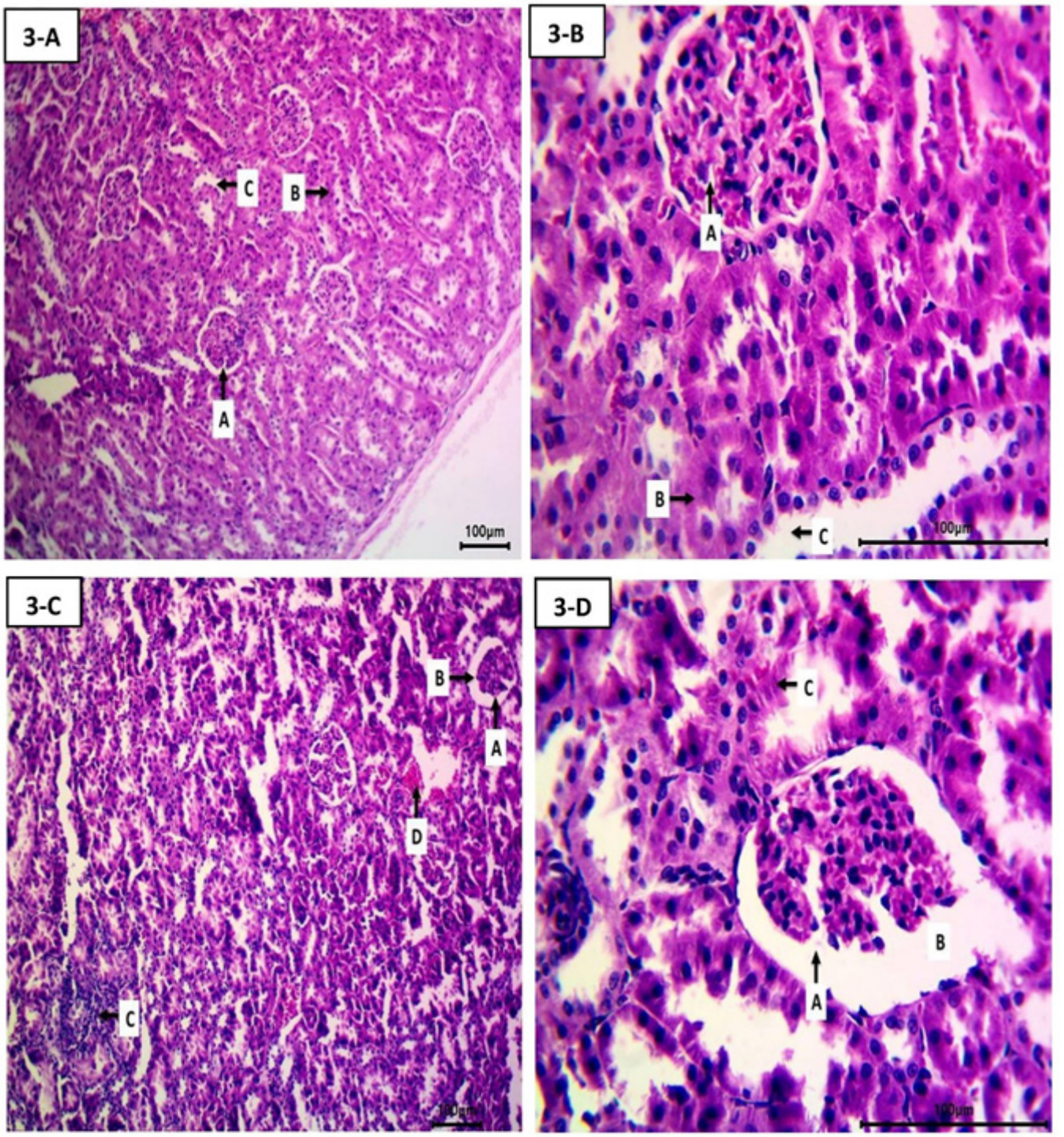

Fig. 3: photomicrograph of rats' kidney tissues (3-A&B): control group showing normal architecture of glomeruli (A), proximal renal tubules (B) and distal renal tubules (C). (3-C): Indian Ginseng treated group showing atrophy of glomeruli (A), dilatation of Bowman's space (B), focal infiltration of inflammatory cells (C) and congestion of blood vessels (D). (3-D): Indian Ginseng treated group showing atrophy of glomeruli (A), dilatation of Bowman's space (B) and coagulative necrosis of epithelial cells lining renal tubules (C). H&E stain (A&C:100X, B&D: 400X).

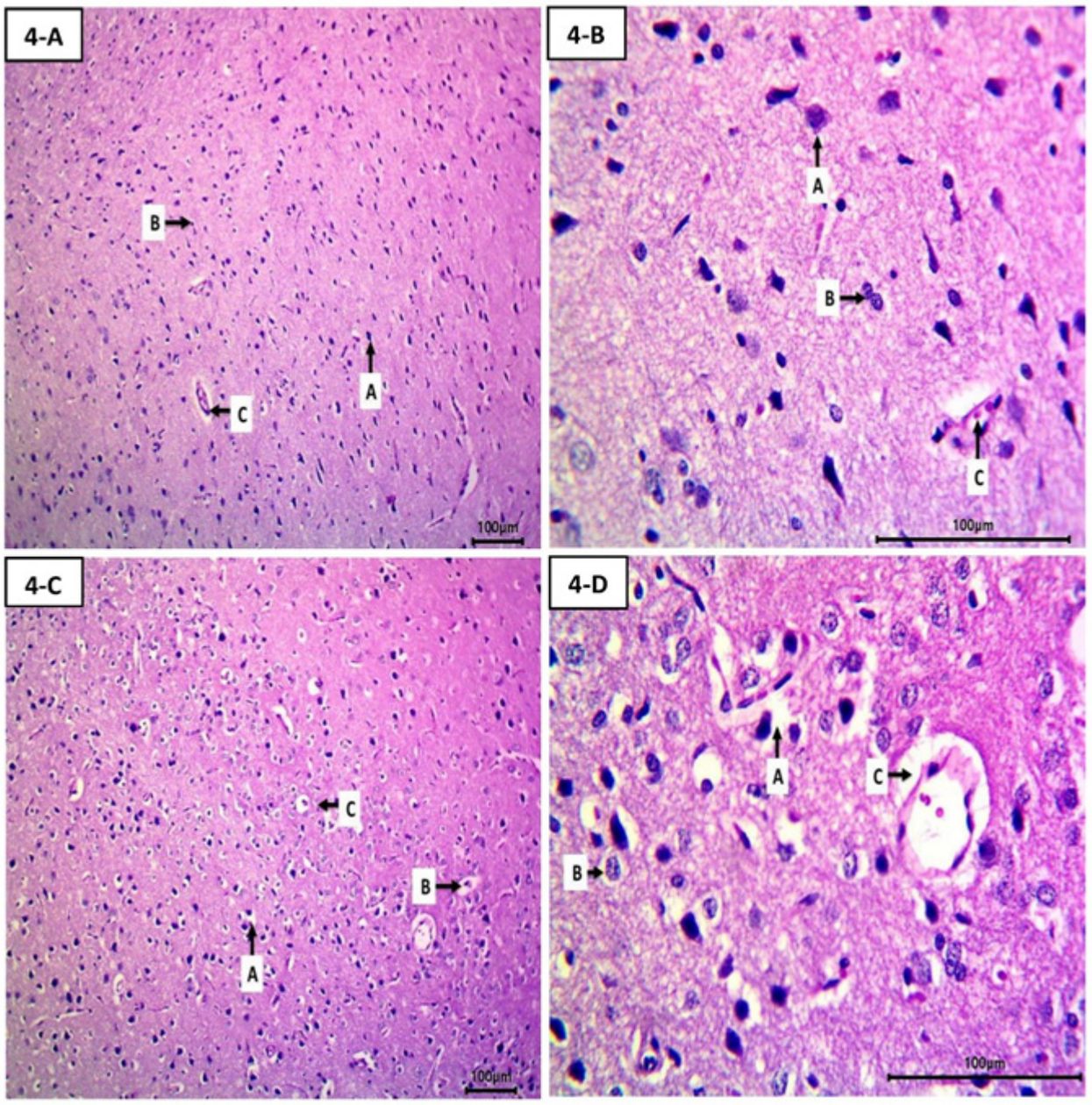

Fig. 4: photomicrograph of rats' brain tissues (4-A&B): control group showing normal architecture representing by normal neurons (A), glial cells (B) and blood vessels (C). (4-C&D): Indian Ginseng treated group showing vacuolization edema surrounding neurons (A) and glial cells (B) as well as perivascular edema (C). H&E stain (A&C:100X, B&D: 400X).

DISCUSSION

Patients all over the world are increasingly using Indian ginseng and other forms of medicinal herbs to treat or prevent various ailments[16,17]. The most difficult difficulty these herbs face is their two potential pharmacological effects (good effect and harmful side effects)[18]. The third challenge is the abundance of these items, which can be obtained easily all over the world and used by anyone due to their generally inexpensive prices[19]. Herbal liver toxicity, or liver damage produced by specific herbs, is typically connected with naturally occurring plants that individuals take[20,21]. Herbal and Ayurvedic remedies have long been thought to be safe and innocuous, but recent evidence suggests that herbs or Ayurveda might induce negative side effects to differing degrees and damage different organs such as the liver[22].

Herbal medicines can cause hepatotoxicity due to a variety of circumstances, including: (a) long-term or high-dose intake of unfamiliar herbs, (b) insufficient and imprecise raw material procurement, resulting in the substitution of beneficial herbs for toxic herbs[23], (c) unintentional or intentional contamination with hepatotoxic non-herbal drugs, (d) potentiation or augmentation of the toxic effects of conventional medicines as a result of interaction with chemicals in the herbal mixture[24].

According to several studies, hepatotoxicity caused by herbal medications is the second most common cause of drug-induced liver injury in Western countries[25]. Another study, which examined data from the California health care system from 2004 to 2014, discovered that usage of herbal medications caused approximately 18.8% of acute liver failure cases[26]. Herbal remedies are the most common cause of "drug-induced liver injury" or "herb-induced" liver injury (HILI) in Eastern countries[27], and a study conducted on the Korean country found that medicinal plants or herbs were the causal effect. It is responsible for 62.5% of documented HILI cases, with 232 of 371 cases detected[28].

Previous European research conducted in Spain between 1994 and 2004 indicated that around 9% of 461 individuals with herb-induced liver injury (HILI) were caused by excessive consumption of medicinal herbs[29]. Group B (Indian ginseng-treated group) liver sections revealed extensive vacuolar degeneration of hepatocytes, inflammatory cell infiltration in the portal area, central vein congestion, and hemosiderin staining. In addition to coagulative necrosis of focal pleomorphic hepatocytes, mononuclear inflammatory cell infiltration in the portal area, and eosinophilic cytoplasmic deposition of hepatocytes, congestion and dilatation, liver sections in this group showed congestion and dilatation of the central vein and portal vein with sinusoidal dilatation. It comes from the portal vein.

These histopathological effects could be attributed to the presence of potentially harmful effects of some biologically active substances found in Indian ginseng, such as withanolides (steroidal lactone triterpenoids) and alkaloids, which are organic nitrogen-containing compounds that are considered a toxic component of many herbal medicines[30]. These substances have been reported to cause anabolic and steroidogenic jaundice[31], and withanolides have also been found to inhibit NF_B activation and NF_B gene activation, which explains their ability to induce apoptosis and necrosis of hepatocytes in some areas of the liver[32,33].

Several investigations back up the aforesaid finding. Although Indian ginseng is usually regarded as a healthy herb, many incidents of liver damage in patients taking herbal products containing Indian ginseng have been observed. These liver lesions emerged 2 to 12 weeks after the commencement of Indian ginseng consumption, with itching and jaundice as a cholestatic damage[34]. A liver biopsy revealed severe intrahepatic cholestasis and acute ductal slurry plugs in the first incidence of hepatotoxicity associated with Indian ginseng. Two months after discontinuing the offending medicine, the patient was cured[35].

Björnsson *et al*. in 2020 also reported that ashwagandha (Indian ginseng) consumption caused drug-induced hepatotoxicity in several patients from the United States and Iceland, and the aforementioned author described 5 patients who developed cholestatic jaundice after taking herbal medicines containing ashwagandha for approximately 2 - 12 weeks. The liver was cholestatic or mixed in nature, and liver biopsies revealed severe cholestatic hepatitis[36]. Group B (Indian ginseng-treated group) kidney sections showed overall glomerular atrophy, dilatation of Bowman's space, localized infiltration of inflammatory cells, and vascular congestion, as well as coagulative necrosis of epithelial cells lining the renal tubules.

Concerning the aforementioned kidney histology results and nephrotoxicity, there has been a considerable body of research over the last 20 years focused on nephrotoxicity produced by taken herbal medications[37]. In these studies, the most nephrotoxic herbal components were aristolochic acids and alkaloid compounds[38]. Long-term ingestion of these alkaloids (found in Indian ginseng) results in significant nephrotoxicity and oxidative damage in rat kidneys[39]. This situation could be caused by the high levels of reactive oxygen species (ROS) generated when these chemicals reach and act on the kidneys, causing direct injury to kidney cells[40,41]. A possible mechanism of kidney damage can also occur when reactive oxygen species react with cell membrane content to produce lipid peroxidation and thus damage the oxidative phosphorylation process, causing energy metabolism to become abnormal, leading to abnormal mitochondrial function, apoptosis, and cell damage[42]. Huang *et al*., 2019 also stated that when (redox and antioxidant balance) is unregulated and disturbed, excess oxygen free radicals are not promptly removed, resulting in the production of "lipid peroxidation damage" and nephrotoxicity in the future[43].

Group B (Indian ginseng-treated group) brain sections revealed vacuolization edema surrounding neurons and glial cells, as well as perivascular edema. The term neurotoxicity refers to the physical damage to brain tissue caused by exposure to a neurotoxin, which is a drug that kills or inactivates neurons and hence changes nervous system activity[44].

Many case studies have demonstrated that herbal drugs might cause cerebral edema, cerebral arteritis, intracerebral hemorrhage, coma, encephalopathy, and other types of cerebrovascular accidents (CVAs). These side effects have occurred due to a variety of factors, including herb toxicity, contaminated herbal preparations, herb and medication interactions, and incorrect or extended usage of these plants[45].

Environmental contamination is one of the leading causes of heavy metal accumulation in plant parts, which eventually enter the human food chain[46]. Several studies have found that Withania somnifera (Indian ginseng) has the highest mineral bioaccumulation when compared to other herbal products[47]. Especially when the iron mineral present in sufficient quantities in Indian ginseng initiates a Fenton reaction, which is characterized by the oxidation of Fe II to Fe III, generating free radicals, followed by the reduction of Fe III and then to Fe I.

Finally, growing evidence suggests that heavy metal-induced neurotoxicity is critical for the induction of reactive oxygen species, which ultimately leads to increased oxidative stress throughout brain tissue, explaining the presence of perivascular discharge edema of neurons and glial cells, as well as perivascular edema, which was also observed in brain sections[48].

CONCLUSION

We concluded that ashwagandha (Indian ginseng) has a negative effects as histological changes in the liver, kidney, and brain organs in rats at the concentration level utilized in the study.

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CONFLICT INTERESTS

There are no conflicts of interest.

REFERENCES

1. Dutta R, Khalil R, Green R, Mohapatra SS, Mohapatra S. Withania Somnifera (Ashwagandha) and Withaferin A: Potential in Integrative Oncology. Int J Mol Sci. (2019) 20(21):5310. DOI:10.3390/ijms20215310.
2. Idrees I, Taqa G, ALtaaye S. The effect of Ashwagandha Versus Amitriptyline on the Histological Structure of Submandibular Glands in Albino Rats. Egypt. J. Vet. Sci. (2023) 54(1):97-107. DOI: 10.21608/EJVS.2022.156115.1381.
3. Park HJ, Kim DH, Park SJ, Kim JM and Ryu JH. "Ginseng in traditional herbal prescriptions". JGR. (2012) 36(3):225-241. doi:10.5142/jgr.2012.36.3.225
4. Pandey MM, Rastogi S, Rawat AK. Indian traditional ayurvedic system of medicine and nutritional supplementation. Evid Based Complement Alternat Med. (2013) 2013:376327. DOI: 10.1155/2013/376327.
5. Singh N, Bhalla M, de Jager P, Gilca M. An overview on ashwagandha: a Rasayana (rejuvenator) of Ayurveda. Afr J Tradit Complement Altern Med. (2011) 8(5):208-213. DOI: 10.4314/ajtcam.v8i5S.9.
6. Gupta S, Bansal RN, Sodhi SP S, Brar GK, Malhotra M. Ashwagandha (Withania somnifera) – a herb with versatile medicinal properties empowering human physical and mental health. J Pre Clin Clin Res. (2021) 15(3):129-133. DOI: 10.26444/jpccr/141582.
7. Paul S, Chakraborty S, Anand U, *et al*. Withania somnifera (L.) Dunal (Ashwagandha): A comprehensive review on ethnopharmacology, pharmacotherapeutics, biomedicinal and toxicological aspects. Biomed Pharmacother. (2021) 143:112175. DOI: 10.1016/j.biopha.2021.112175.
8. Afewerky HK, Ayodeji AE, Tiamiyu BB, *et al*. Critical review of the Withania somnifera (L.) Dunal: ethnobotany, pharmacological efficacy, and commercialization significance in Africa. Bull Natl Res Cent. (2021) 45(1):176. DOI: 10.1186/s42269-021-00635-6.
9. Chandrasekhar K, Kapoor J, Anishetty S. A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of ashwagandha root in reducing stress and anxiety in adults. Indian J Psychol Med. (2012) 34(3):255-262. DOI: 10.4103/0253-7176.106022.
10. Auddy B, Hazra J, Mitra A, Abedon B, Ghosal S. A standardized Withania somnifera extract significantly reduces stress-related parameters in chronically stressed humans: A double-blind, randomized, placebo-controlled study. J Am Nutraceutical Assoc. (2008) 11:50-56. DOI: 10.1.1.324.8921.
11. Feige-Diller J, Krakenberg V, Bierbaum L, *et al*. The Effects of Different Feeding Routines on Welfare in Laboratory Mice. Front Vet Sci. (2020) 6:479. DOI: 10.3389/fvets.2019.00479.
12. Alhahawachee Z, Taqa G, & Al Allaf L. Ashwagandha Roots Extract Attenuate Some Anatomical and Behavioral Outcomes in Rat' Pups After Early Postnatal Induction of Hypothyroidism. Egypt. J. Vet. Sci. (2023) 54(1):31-46. DOI: 10.21608/ejvs.2022.148653.1361.

13. Mahmoud GS, Ahmed AH, Kassim BM. Assessment of histopathological and hematological changes in mice treated with the aqueous extract of origanum (Driganum majorana. L) in algabal Alakhder libya. AJMS. (2022) 1(1):12-17. DOI: https://doi.org/10.55145/ajbms.2022.1.1.003.

14. Al-Jammas S. Nephrotoxicity Induced by Cytosar in Rabbits Kidneys (A Histological Study). Am. J. Biomed. Res. (2019) 7(1):1-5. DOI:10.12691/ajmbr-7-1-1.

15. Al-Jammas S., Al-Saraj A. The histological changes induced by Cytarabine on rabbits livers (with and without vitamin E administration). Iraqi J Vet Sci (2020) 34(1): 9-13. doi: 10.33899/ijvs.2020.163564.

16. Teschke, R.; Eickhoff, A. Herbal hepatotoxicity in traditional and modern medicine: Actual key issues and new encouraging steps. Front. Pharmacol. (2015) 23(6):72. DOI: 10.3389/fphar.2015.00072.

17. Telles, S.; Pathak, S.; Singh, N.; Balkrishna, A. Research on Traditional Medicine: What Has Been Done, the Difficulties, and Possible Solutions. Evidence-Based Complementary and Alternative Medicine. Hindawi Publ. Corp. (2014) 2014, 495635. DOI: https://doi.org/10.1155/2014/495635.

18. Taqa, G. A., & Idrees, I. R. Evaluation the effect of amitriptyline and/or ashwagandha on body weight in male rats. AJMS. (2023) 2(1):28-33. DOI: https://doi.org/10.55145/ajbms.2023.1.1.005.

19. Firenzuoli, F.; Gori, L. Herbal Medicine Today: Clinical and Research Issues. Evid.-Based Complementary Altern. Med. (2007) 4:37-40. DOI: 10.1093/ecam/nem096.

20. Teschke R, Frenzel C, Glass X, Schulze J, Eickhoff A. Herbal hepatotoxicity: a critical review. Br J Clin Pharmacol. (2013) 75(3):630-636. DOI: 10.1111/j.1365-2125.2012.04395.x.

21. Chalasani NP. Hayashi PH, Bonkovsky HL, Navarro VJ, Lee WM, Fontana RJ. ACG Clinical Guideline: The Diagnosis and Management of Idiosyncratic Drug-Induced Liver Injury. Am. J. Gastroenterol. (2014) 109:950-966. DOI: 10.1038/ajg.2014.131.

22. Başaran N, Paslı D, Başaran AA. Unpredictable adverse effects of herbal products. Food Chem Toxicol. (2022) 159:112762. DOI: 10.1016/j.fct.2021.112762.

23. Teschke R, Frenzel C, Glass X, Schulz J, Eickoff A. Herbal hepatotoxicity: A critical review. Br. J. Clin. Pharmacol. (2013) 75:630-636. DOI: 10.1111/j.1365-2125.2012.04395.x.

24. Amadi CN, Orisakwe OE. Herb-Induced Liver Injuries in Developing Nations: An Update. Toxics. (2018) 6(2):24. DOI: 10.3390/toxics6020024.

25. Stournaras E, Tziomalos K. Herbal medicine-related hepatotoxicity. World J Hepatol. (2015) 7(19):2189-2193. DOI: 10.4254/wjh.v7.i19.2189.

26. Goldberg DS, Forde KA, Carbonari DM, Lewis JD, Leidl KB, Reddy KR, Haynes K, Roy J, Sha D, Marks AR, *et al*. Population-representative incidence of drug-induced acute liver failure based on an analysis of an integrated health care system. Gastroenterology. (2015) 148:1353-1361.e3. DOI: 10.1053/j.gastro.2015.02.050.

27. Amadi CN, Orisakwe OE. Herb-Induced Liver Injuries in Developing Nations: An Update. Toxics. (2018) 6(2):24. DOI: 10.3390/toxics6020024.

28. Suk KT, Kim DJ, Kim CH, Park SH, Yoon JH, Kim YS, Baik GH, Kim JB, Kweon YO, Kim BI, *et al*. A prospective nationwide study of drug-induced liver injury in Korea. Am J Gastroenterol. (2012) 107:1380–1387. DOI: 10.1038/ajg.2012.138.

29. Andrade RJ, Lucena MI, Fernández MC, Pelaez G, Pachkoria K, García-Ruiz E, García-Muñoz B, González-Grande R, Pizarro A, Durán JA, *et al*. Drug-induced liver injury: an analysis of 461 incidences submitted to the Spanish registry over a 10-year period. Gastroenterology. (2005) 129:512–521. DOI: 10.1016/j.gastro.2005.05.006.

30. Xu X, Zhu R, Ying J, Zhao M, Wu X, Cao G, Wang K. Nephrotoxicity of Herbal Medicine and Its Prevention. Front Pharmacol. (2020) 15(11):569551. DOI: 10.3389/fphar.2020.569551.

31. Delladetsima K, Manesis E, Tiniakos D, Sakellariou S. Complex liver injury induced by combined Aloe Vera and vitamin A oral supplements, as assessed by histology and the updated RUCAM. Explor Med. (2022) 3:181-187 doi.org/10.37349/emed.2022.00084

32. Ichikawa H, Takada Y, Shishodia S, Jayaprakasam B, Nair MG, Aggarwal BB. Withanolides potentiate apoptosis, inhibit invasion, and abolish osteoclastogenesis through suppression of nuclear factor-kappaB (NF-kappaB) activation and NF-kappaB-regulated gene expression. Mol Cancer Ther. (2006) 5(6):1434-1445. DOI: 10.1158/1535-7163.MCT-06-0096.

33. Idrees IR, Taqa GA, Ibrahim SK. Acetylcholine Esterase Gene Expression in Salivary Glands of Albino Rats after Treatment with amitriptyline or/and Ashwagandha. JAVS. (2023) 8(1): 72-77. DOI: 10.21608/javs.2022.173225.1191.

34. Lubarska M, Hałasiński P, Hryhorowicz S, Mahadea DS, Łykowska-Szuber L, Eder P, Dobrowolska A and Krela-Kaźmierczak I. Liver Dangers of Herbal Products: A Case Report of Ashwagandha-Induced Liver Injury. Int J Environ Res Public Health (2023) 20(5):3921. https://doi.org/10.3390/ijerph20053921

35. Inagaki K, Mori N, Honda Y, Takaki S, Tsuji K, Chayama K. A case of drug-induced liver injury with prolonged severe intrahepatic cholestasis induced by Ashwagandha. Kanzo. (2017) 58:448–454. DOI: 10.2957/kanzo.58.448.

36. Björnsson HK, Björnsson ES, Avula B, Khan IA, Jonasson JG, Ghabril M, Hayashi PH, Navarro V. Ashwagandha-induced liver injury: A case series from Iceland and the US Drug-Induced Liver Injury Network. Liver Int. (2020) 40:825-829. DOI: 10.1111/liv.14393.

37. Yang B, Xie Y, Guo M, Rosner MH, Yang H, Ronco C. Nephrotoxicity and Chinese Herbal Medicine. Clin J Am Soc Nephrol. (2018) 13(10):1605-1611. DOI: 10.2215/CJN.11571017.

38. Xu XL, Yang LJ, Jiang JG: Renal toxic ingredients and their toxicology from traditional Chinese medicine. Expert Opin Drug Metab Toxicol. (2016) 12: 149-159. DOI: 10.1517/17425255.2016.1132306.

39. Rui Y, Li S, Luan F, Li D, Liu R, Zeng N. Several Alkaloids in Chinese Herbal Medicine Exert Protection in Acute Kidney Injury: Focus on Mechanism and Target Analysis. Oxid Med Cell Longev. (2022) 13:2427802. DOI: 10.1155/2022/2427802.

40. Al-Jammas S., Al-Sarraj A. The histological changes induced by cytarabine on rabbits kidneys (with and without vitamin E administration). Iraqi J Vet Sci. (2019) 33(2): 311-316. doi: 10.33899/ijvs.2019.162910.

41. Xu X, Zhu R, Ying J, Zhao M, Wu X, Cao G, Wang K. Nephrotoxicity of Herbal Medicine and Its Prevention. Front Pharmacol. (2020) 15;11:569551. DOI: 10.3389/fphar.2020.569551.

42. Huang W, Sun R. Pathological Damage Mechanism of Rats' Nephrotoxicity caused by Alcohol Extracted Components of Herbal Leonuri. Chin. J. Exp. Tradit. Med. Formulae. (2017) 16:111-114. DOI: 10.13422/j.cnki.syfjx.2010.09.070.

43. Huang W, Liu C, Xie L, Wang Y, Xu Y, Li Y. Integrated network pharmacology and targeted metabolomics to reveal the mechanism of nephrotoxicity of triptolide. Toxicol. Res. (2019) 8: 850-861. DOI: 10.1039/c9tx00067d.

44. Bilge, Serap. Neurotoxicity, Types, Clinical Manifestations, Diagnosis and Treatment. Neurotoxicity - New Advances, IntechOpen, Mar. (2022) Crossref. DOI: 10.5772/intechopen.101737.

45. Ernst E. Serious psychiatric and neurological adverse effects of herbal medicines -- a systematic review. Acta Psychiatr Scand. (2003) 108(2):83-91. DOI: 10.1034/j.1600-0447.2003.00158.x.

46. Jaishankar M, Tseten T, Anbalagan N, Mathew BB and Beeregowda KN. Toxicity, mechanism and health effects of some heavy metals. Interdisciplinary toxicology. (2014) 7(2):60-72. https://doi.org/10.2478/intox-2014-0009.

47. Kulhari A, Sheorayan A, Bajar S, Sarkar S, Chaudhury A, Kalia RK. Investigation of heavy metals in frequently utilized medicinal plants collected from environmentally diverse locations of north western India. Springerplus. (2013) 17(2):676. DOI: 10.1186/2193-1801-2-676.

48. Fadia BS, Mokhtari-Soulimane N, Meriem B, Wacila N, Zouleykha B, Karima R, Soulimane T, Tofail SAM, Townley H, Thorat ND. Histological Injury to Rat Brain, Liver, and Kidneys by Gold Nanoparticles is Dose-Dependent. ACS Omega. (2022) 7(24): 20656-20665. DOI: 10.1021/acsomega.2c00727.

الملخص العربى

التغيرات النسيجية التي تحدثها عشبة الجنسنج الهندي في انسجة الكلى والاكباد والادمغة في الجرذان

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مقدمه: لا تتم مراقبة استخدام المستحضرات العشبية بشكل جيد، فهي لا تخضع لنفس اختبارات الأدوية الكيميائية أثناء التصنيع ولا توجد معايير واضحة كتلك الموجودة بالأدوية الطبية لهذا فان استخدامها دون قيود او شروط قد يحدث تأثيرات غير مرغوبة او سمية على الأعضاء المختلفة.

هدف البحث: أجريت هذه الدراسة للبحث في بعض التأثيرات الضارة لاستخدام عشبة الاشواكندة (الجنسنج الهندي) وتأثيراتها المحتملة على الانسجة التابعة لاعضاء الكبد والكلية والدماغ.

مواد و أساليب العلاج: تم تقسيم ١٦ جرذاً بالغاً عشوائياً لمجموعتين ٨ / مجموعة، المجموعة الأولى هي مجموعة السيطرة التي تم إعطاؤها ماء مقطر يومياً عن طريق الفم لمدة ٣٠ يومًا، بينما المجموعة الثانية كانت المجموعة المعالجة بالجنسنج الهندي والتي تم إعطاؤها مستخلص جذور الجنسنج الهندي بجرعة (٢٠٠ ملغم/كغم) مخففة في (١,٠ مل من الماء المقطر) عن طريق الفم يوميًا ولمدة ٣٠ يومًا. بعد نهاية مدة المعالجة تم تخدير الحيوانات واخذت منها أعضاء الكبد والكلية والدماغ لملاحظة التغييرات النسجية المرضية الملاحظة في تلك الانسجة.

النتائج: سجلت النتائج في أقسام الكبد في المجموعة المعالجة تنكس فجوي منتشر لخلايا الكبد، وارتشاح الخلايا الالتهابية في منطقة الباب، واحتقان الوريد المركزي وتصبغ الهيموسيديرين وكذلك احتقان وتوسع الوريد المركزي والوريد البابي مع توسع الجيبانيات. بينما أظهرت أقسام الكلى لنفس المجموعة ضمور الكبيبات وتوسع حيز بومان وارتشاح الخلايا الالتهابية البؤرية واحتقان الأوعية الدموية. أخيرًا، أظهرت انسجة أدمغة المجموعة المعالجة وذمة تفريغ محيطة بالخلايا العصبية والخلايا الدبقية بالإضافة إلى وذمة حول الأوعية الدموية.

الاستنتاج: خلصت الدراسة الى وجود تأثيرات نسيجية ضارة للاشواكندة (الجنسنج الهندي) في بعض أعضاء الجرذان ضمن الجرعة المستخدمة في الدراسة مما يستدعي المزيد من الدراسات في هذه العشبة لتحديد الجرع غير الضارة عند استخدامها.